In recent years it has been established that a local synthesis of virus antibodies in the central nervous system (CNS) takes place in many multiple sclerosis (MS) patients. The following is an attempt to focus attention on some aspects of the locally synthesized virus antibodies in MS and some infections of the nervous system, their relation to locally synthesized IgG, and their possible biological significance. A more detailed review of virus antibodies in MS has recently been published elsewhere [16].

**Local Synthesis of IgG in the CNS**

Kabat et al. [6] were the first to demonstrate a selective increase of the γ-globulin fraction of the CSF in patients with MS and neurosyphilis. The association between this increase and a local synthesis of IgG within the CNS in MS was established by Frick and Scheid-Seydel [3]. With the advent of high-resolution electrophoretic methods, such as agar- or agarose-gel electrophoresis, it has been established that local IgG synthesis is reflected in the occurrence of oligoclonal IgG in the CSF in a variety of CNS infections and in 80–90% of MS patients [8, 10, 12].

**Local Synthesis of Viral Antibodies in CNS Infections**

Subacute sclerosing panencephalitis (SSPE), a disease of children and adolescents caused by a measles virus infection of the brain, is regularly associated with a local synthesis of oligoclonal IgG [8, 12]. Several lines of evidence indicate that a local synthesis of measles antibodies takes place in this disease [21, 23]. Results from serological studies of IgG separated by electrofocusing [7], preparative agarose electrophoresis [17, 26], and immunoelectrophoresis [24] indicate that locally synthesized measles antibodies in SSPE are associated with the fractions of oligoclonal IgG in the CSF. Final proof of this association has been provided by specific absorption of the oligoclonal IgG of brain extract and CSF samples by measles virus antigens, and by the subsequent recovery of corresponding oligoclonal measles antibodies by acid elution of the antigen-antibody complexes formed by the absorption [27]. These
data indicate that the occurrence of oligoclonal IgG in the CSF of patients with SSPE reflects a specific antibody response to the presence of measles virus antigens in the CNS.

Evidence for an association of oligoclonal IgG with virus-specific antibody activities has also been reported in chronic progressive rubellavirus panencephalitis [29] and mumps meningitis [30]. Recent work in patients with neurosyphilis has shown that the bulk of the oligoclonal IgG of the CSF represents antibody to *Treponema pallidum* (Vandvik, unpublished data). Thus, in these infectious diseases the bulk of the oligoclonal IgG synthesized locally in the CNS may also be explained as a specific antibody response to the causal agent.

**Local Synthesis of Viral Antibodies in MS**

Raised levels of measles antibodies in serum and CSF of patients with MS were first reported by Adams and Imigawa [1]. The unraveling of the role of measles virus in SSPE gave a boost to theories concerning measles virus as an etiological agent in MS. Evidence for a local synthesis in the CNS of measles antibodies in this disease was first provided by Salmi et al. [21]. Their work was based on the demonstration of serum/CSF quotients of measles antibodies which were significantly lower than corresponding quotients for other antibodies. Work along the same lines has since confirmed these findings [2, 5, 18, 19, 22, 25]. A local measles antibody synthesis in the CNS takes place in approximately 60% of MS patients [18, 19] and in up to 30% of patients with optic neuritis [11, 13].

In additional studies, analyses were made of antibodies to several different viruses in serum and CSF samples from 150 Scandinavian MS patients [19]. A local synthesis of measles antibodies was found in 57%, of rubella antibodies in 19%, of mumps antibodies in 15%, of antibodies to herpes simplex type 1 virus in 11%, and of antibodies to parainfluenza virus type 1 (Sendai) in 3%. A local production of antibodies to any one of the viruses was found in 71% of the patients. This included 48, 16, and 7% of patients who had a local synthesis in the CNS of antibodies to one, two, and three or more viruses, respectively.

Low serum/CSF quotients for antibodies to rubellavirus in MS have been reported in other studies [9, 22] and indications of a local synthesis of herpes simplex antibodies in one study [5].

The occurrence of low measles antibody quotients is correlated with the occurrence of oligoclonal IgG in the CSF of patients with MS [18, 19, 25] and optic neuritis [10]. Indications of an electrophoretic restriction of the locally synthesized measles antibodies have been reported based on serological studies of IgG separated by preparative electrophoresis [17] and by immunoelectrophoresis [25]. More recently, absorption-elution experiments have shown that the locally synthesized measles antibodies in MS are indeed of an oligoclonal nature [27]. However, these experiments showed that the locally synthesized measles antibodies were not associated with the major fractions of oligoclonal IgG in the CSF demonstrable by agarose electrophoresis.

Previously available methods have not allowed the investigation of an association of the oligoclonal IgG of the CSF in individual MS patients with antibody ac-